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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/017,135	12/07/2001	Neil Russell Foster	HILLS1100	8942
28213	7590	01/11/2008	EXAMINER	
DLA PIPER US LLP			OH, SIMON J	
4365 EXECUTIVE DRIVE			ART UNIT	
SUITE 1100			PAPER NUMBER	
SAN DIEGO, CA 92121-2133			1618	
			MAIL DATE	DELIVERY MODE
			01/11/2008	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

**Office Action Summary**

Application No.

10/017,135

Applicant(s)

FOSTER ET AL.

Examiner

Simon J. Oh

Art Unit

1618

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 25 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-20,28 and 30-35 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-20,28 and 30-35 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Papers Received***

Receipt is acknowledged of the applicant's amendment, response, and request for continued examination, all received on 25 October 2007.

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 25 October 2007 has been entered.

### ***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejection of Claims 1-20 under 35 U.S.C. 103(a) over Debendetti *et al.* (U.S. Patent No. 6,063,910) in view of Merrified *et al.* (PCT Publication No. WO 00/37169) is maintained.

Claims 28 and 30-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Debendetti *et al.* (U.S. Patent No. 6,063,910) in view of Merrified *et al.* (PCT Publication No. WO 00/37169)

The Debendetti *et al.* patent teaches processes for producing microparticles from a solution by anti-solvent re-crystallization using a supercritical fluid (See Column 2, Lines 22-30). Preferred anti-solvent fluids include ethane and ethylene (See Column 2, Lines 39-43). The microparticles can be produced with particle sizes of less than 10 microns (See Column 2, Lines 61-66). In one embodiment, a solution of a soluble material in a solvent is passed through a continuum of supercritical fluid, whereby the soluble material precipitates. The solution may be passed through in the form of droplets, a thin film, or a plurality of fine streams (See Column 2, Lines 44-55). The anti-solvent is introduced at temperatures ranging from 25° to 45°C and 60 to 200 atm (See Column 5, Lines 33-41). The resulting precipitated particles may then be collected on a suitable collection means (See Column 5, Lines 19-22). The disclosed processes may be used to make particles of proteins, such as insulin (See Example 2; and Claim 8).

The Debendetti *et al.* patent does not disclose the use of a modifying agent in the anti-solvent.

The Merrified *et al.* publication discloses a process and apparatus for the production of particles using a solvent/anti-solvent process in which the anti-solvent is preferably a supercritical fluid (See Abstract). Suitable anti-solvents include ethane and ethylene. The anti-solvent stream may further comprise a modifier, such as methanol and ethanol. Such modifiers alter the intrinsic properties of the supercritical anti-solvent at or around the critical point (See Page 5, Line 19 to Page 6, Line 4). The compressible anti-solvent may be introduced at pressures of 50 to 100 bar at a suitable temperature, which is likely to be in the range of 1.01  $T_C$  to 4.0  $T_C$  (See Page 6, Lines 5-12; and Page 12, Lines 19-25). The apparatus may include a means for collection of the particles, such as a collection chamber (See Page 16, Line 21-29).

The particles may be a pharmaceutical material, with a small particle size, such as around 1 to 20 microns (See Page 18, Lines 7-9).

It would be obvious for one of ordinary skill in the art to combine the disclosures of the prior art in order to obtain the instantly claimed invention. One of ordinary skill in the art would seek to exert a greater degree of control over the processes disclosed by Debendetti *et al.* by the use of modifying agents in the supercritical anti-solvent, as taught by Merrified *et al.* As both prior art references deal with solvent/anti-solvent precipitation processes using a supercritical fluid, they are considered to be analogous art. Therefore, one of ordinary skill in the art would be able to combine the disclosures of the prior art with a reasonable expectation of success. The Debendetti *et al.* discloses that particles are formed when a solution of the material is passed through a continuum of an anti-solvent stream, which is seen by the examiner as reading on the claim limitation that particles are formed upon the contact of a solvent stream with an anti-solvent stream. Thus, the instantly claimed invention is *prima facie* obvious.

#### ***Response to Arguments***

Applicant's arguments filed 25 October 2007 have been fully considered but they are not persuasive.

The applicant first argues that the prior art teaches away from the use of an aqueous solvent, according to its interpretation of the Debendetti *et al.* However, that reference clearly states that aqueous solvents can be used, with the explicitly predictable result that it will result in a lower yield. However, this should not be interpreted as resulting in an inoperable embodiment. It should instead be interpreted as a non-preferred embodiment, which still remains applicable

against the instant claims. There may be various reasons as to why the use of an aqueous solvent may be used even though it may result in a lower yield such as environmental concerns or cost considerations. That choice is left to those of ordinary skill in the art, to adapt prior art processes to the particular need at hand.

Next, the applicant argues that unpredictability of the art makes it so that the prior art references cannot be combined with any reasonable level of predictability.

The declaration under 37 CFR 1.132 filed 25 October 2007 is insufficient to overcome the rejection of Claims 1-20 based upon obviousness as set forth in the last Office action because: the showing is not commensurate in scope with the instant claims.

First, Dr. Tu's declaration cites the Ting *et al.* article, stating that the solubility of naproxen varied non-linearly at high co-solvent concentrations. However, non-linear behavior is not necessarily unpredictable, if a proper model can be found to account for this trend. Furthermore, the instantly claimed invention is not directed only towards the production of naproxen particles.

Second, Dr. Tu cites the Hutcherson and Foster reference, which attempts to describe the difficulties in adequately and quantitatively predicting SCF behavior. However, this reference was published in 1995, drawing from information presented at a symposium held in November 1994. Therefore, it is unclear as to whether the information presented in that reference remained an accurate description of the state of the art at the time the instant application was filed, in this country in December 2001 and in Australia in December 2000.

Finally, Dr. Tu cites the Jouyban *et al.* article, stating that the solubility of nicotinic acid and p-acetoxycetanilide in supercritical carbon dioxide provided varying results in experimental

error, and thus concluded that a large amount of uncertainty exists in supercritical fluid processes. However, that same reference showed that the global AARD was 12.6% with their best model, well within the range of acceptable error.

Dr. Tu also based her opinion on a rather narrow interpretation of the prior art, characterizing the use of an aqueous solvent as one of two changes that are alleged to be needed to adapt the prior art to the instantly claimed invention. The Debendetti *et al.* is very clear that the use of water results in an operable species, even if it results in a lower yield. Therefore, the predicted outcome involves only one change to be analyzed.

As the declaration is not persuasive, and as the applicant's other arguments are not persuasive, the pending claims are rejected.

### ***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Simon J. Oh whose telephone number is (571) 272-0599. The examiner can normally be reached on M-F 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Simon J. Oh  
Examiner  
Art Unit 1618

sj0

A handwritten signature in black ink, appearing to read 'Michael G. Hartley', with a large, stylized flourish at the end.

MICHAEL G. HARTLEY  
SUPERVISORY PATENT EXAMINER